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June 28, 2004

*VIA FEDERAL EXPRESS*

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1061
5630 Fishers Lane
Rockville, MD 20852

**RE: Docket Number 2004P-0075**

Dear Sir/Madam:

The undersigned, Mylan Pharmaceuticals Inc. ("Mylan"), submits this supplement to its citizen petition, dated February 17, 2004 (the "Petition"), filed under § 505 of the Federal Food, Drug, and Cosmetic Act ("FDCA") and 21 C.F.R. §§ 10.25 and 10.30. In that Petition, Mylan urged FDA to end the practice of marketing so-called "authorized generics" during the 180-day generic drug exclusivity that Congress created as part of the Hatch-Waxman Amendments to the FDCA (the "180-day exclusivity"). 21 U.S.C. § 355(j)(5)(B)(iv).

The purpose of this supplement is to respond to the Comment filed by Johnson & Johnson ("J&J") on May 11, 2004 opposing the Petition, and to urge FDA to render a decision on the Petition as soon as possible.

As explained in the Petition and in the supporting Comments of Apotex Inc., the Generic Pharmaceutical Association, and Teva Pharmaceuticals USA, Inc., the marketing of authorized generics during the 180-day exclusivity "is contrary to the letter and intent of the law," and FDA "has an obligation to implement a policy which is consistent with existing laws and regulations, to prohibit the marketing and distribution of authorized generics until the expiration of the [180-day exclusivity]." Petition at 1 and 3.

To date, FDA has not yet responded to Mylan's Petition dated February 17, 2004. In the meantime, however, brand name companies have continued to announce the launch, and have actually launched, "authorized generics" during the 180-day generic drug exclusivity of various ANDA-filing generic companies, including Mylan.

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In particular, on or about March 24, 2004, under license from The Procter & Gamble Company ("P&G"), Watson Pharmaceuticals, Inc. ("Watson") launched an


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authorized generic version of Macrobid (nitrofurantoin monohydrate/macrocrystals), on the very same day that Mylan launched its own generic nitrofurantoin for which it holds the 180-day exclusivity.

**The FDCA and the Regulations Do Not Allow Authorized Generics**

***The FDCA Does Not Allow Authorized Generics***

Contrary to what J&J asserts, the FDCA does not *allow* the marketing of authorized generics during the 180-day exclusivity. Both the courts and the FDA have interpreted section 505(j)(5)(B)(iv) in a broad and purposefully manner that upholds "the statute's interest in affording market access and incentives for both generic and non-generic makers," including by "avoid[ing] an interpretation that excessively favors the first generic and the innovator parties' 'anticompetitive hold' over the drug." *Mylan Pharmaceuticals, Inc. v. Henney*, 94 F. Supp. 2d 36 (D.D.C. 2000).

The marketing of authorized generics during the 180-day exclusivity is anathema to the purpose and workings of the Hatch-Waxman Amendments. J&J's contention that the FDA has no authority to address this practice is baseless, and contrary to past Agency practice. For example, in August 2003, the Agency issued a Final Rule which limited another abuse by brand name companies: the frivolous listing of patents to obtain automatic 30-month stays. The statute (21 U.S.C. § 505(j)) permitted brand companies to obtain multiple automatic 30-month stays for any timely listed patent for which a generic applicant filed a paragraph IV certification.[1] Brand companies would list patents just as a generic applicant was eligible for final approval in order to deter generic competition.

The Agency exercised its authority to issue a final rule to immediately stop this practice by limiting the number of automatic 30-month stays to one per generic application. *FDA Final Rule*, 68 Fed. Reg., No. 117, at 36675 (June 18, 2003).[2] Additionally, the FDA amended its patent submission and listing requirements for new drug applications ("NDAs"). *Id.* "The [f]inal [r]ule will prevent brand companies from submitting certain new patent claims that are unlikely to represent substantial new innovation in order to extend their marketing protection, thus delaying the approval of a generic equivalent." *FDA Statement, FDA's New Regulation to Speed Access to Lower Cost Generic Drugs About to Take Effect*, (August 8, 2003). Clearly, the Agency had the authority to stop a practice which was directly contrary to the spirit and intent of the Hatch-Waxman Amendments.

***FDA's Response to Teva's Citizen Petition Regarding Nifedipine Does Not Allow Authorized Generics***

J&J's reading of FDA's 2001 response to Teva's citizen petition concerning nifedipine is also inaccurate. *FDA Response to Teva's Citizen Petition*, Docket No. 00P-

[1] Medicare Prescription Drug, Improvement and Modernization Act (MMA) of 2003 essentially codified the Agency's rule of limiting automatic 30-month stays to 1 per generic application.

[2] In this case, it is not necessary for the Agency to engage in rule making: the Agency has the ability to restrain the unlawful erosion of exclusivity by answer to Mylan's Petition, issuance of a guidance document, or direct enforcement of existing regulation as applicable. 5 U.S.C. § 553(b)(3)(B).

1446/CP1 (Feb. 6, 2001). The proper interpretation of that case has already been put forward in the Petition and the supporting Comments of Apotex and Teva. Suffice it to say that contrary to J&J's assertion at page 3 of its Comment, Mylan did not change its paragraph IV into a paragraph III certification after settling with Pfizer. Rather, FDA exercised it authority to determine that Mylan's commercial marketing of the authorized generic version of Pfizer's 30mg Nifedipine tablets triggered the 180-day exclusivity.

The basis of the Agency's decision was that the marketing of an authorized generic during the 180-day exclusivity period is the same as the marketing of a true generic drug. Even the District Court noted this as it stated, "whether Mylan markets the produc[t] approved in its ANDA or the produc[t] is Pfizer's NDA is of little import to the statutory scheme; Mylan has begun commercial marketing of gene[r]ic nifedipine, permitting Mylan to market nifedipine without triggering the 180-day exclusivity would be inconsistent with the intent of the statutory scheme." *Mylan Pharmaceuticals Inc. v. Tommy G. Thompson, et al.*, 207 F. Supp. 2d 476 (N.D.WV. 2001). In the same manner, the marketing of an authorized generic drug during the 180-day exclusivity is in substance, or can be analogized to, the marketing of an ANDA-approved drug because the sale of the authorized generic only occurs upon the marketing of the first applicant's product, following a 180-day exclusivity triggering event.

There is nothing in the statute which expressly allows a brand company to manipulate its NDA into the legal equivalent of a generic drug application without prior Agency review of the changes. In fact, the statute requires that major changes to a NDA only be made upon submission of a prior approval supplement. 21 U.S.C. § 506a. Surely, converting a NDA into the legal equivalent of a generic drug application constitutes a major change.

***Applicable Regulations Do Not Allow Authorized Generics***

Brand companies that have converted their NDAs into generic drugs without prior Agency approval wrongfully rely on 21 C.F.R. § 314.70 to make this conversion. FDA issued these regulations and related guidance documents outlining changes which can be made to a NDA with and without prior Agency approval based on the FDA's limited resources. The Agency never contemplated this manipulation by brand companies of the regulations.

For example, in order to allow Watson to launch its authorized generic Macrobid, P&G manufactured Macrobid capsules with a different appearance, namely a different engraved imprint. In addition, P&G packaged these capsules under a different labeling which omits any reference to P&G or Macrobid's NDC, and replaces this information with Watson's name and Watson's NDC for "generic" Macrobid.

Brand companies notify the Agency of the changes in their annual reports based upon the following provisions of the regulations:

1. A change in the labeling concerning the description of the drug product or in the information about how the drug product is supplied, that does not

involve a change in the dosage strength or dosage form. 21 C.F.R. § 314.70(d)(2).

2. An editorial or similar minor change in the labeling. 21 C.F.R. § 314.70(d)(3).

3. The deletion of an ingredient intended only to affect the color of the drug product. 21 C.F.R. § 314.70(d)(4).

4. The addition by embossing, debossing, or engraving of a code imprint to a solid oral dosage form drug product other than a modified release dosage form, or a minor change in an existing code imprint. 21 C.F.R. § 314.70(d)(9).

Brand companies do not stop there. They also market the converted product in the generic segment of the market as an ANDA drug while continuing to detail and market the identical product without any changes as a brand product. In order to compete in the generics market, brand companies also eliminate the true manufacturer of the product from the labeling usually by designating a subsidiary as the manufacturer, but only for the authorized generic product.

FDA did not promulgate section 314.70(d)(2) to allow brand companies to market two different forms of the identical product for the sole purpose of extending its monopoly. Rather, the regulations were implemented in order to provide brand manufacturers the flexibility to make routine changes to the labels on their drug products.

It cannot be argued that the FDA intended its regulations to provide an avenue to sell a generic drug which directly competes with the first generic applicant that holds the 180-day exclusivity. In fact, the statute does not permit these changes; rather it requires a supplement to the NDA to be approved by the Agency prior to making any major changes. *See* 21 U.S.C. §506a. Even if these changes are permitted, contrary to J&J's assertion on page 2 of its Comment, these are not routine changes which ensure that FDA approved products are widely distributed. If that was the case, the changes would be made to the entire product line and the brand company would not go through additional hurdles in order to compete in the generic segment of the market. Therefore, in its Petition, Mylan provided the Agency with alternatives to end this practice – implement an abbreviated application process or require the listing of the drug prior to marketing and distribution.

J&J argues that Mylan's proposals are unlawful, however, J&J fails to point to any provision of the statute which prohibits the FDA from adopting these concepts. In fact, the Agency used to accept similar applications and there is nothing in the statute which would prohibit the Agency from accepting these applications now. Even FDA's current regulations provide the agency with discretion in accepting such applications. 21 C.F.R. 314.101. Section 314.101 expressly provides the FDA with discretion in accepting for filing certain applications for drug products that are already covered by an

approved application. FDA promulgated section 314.101 in order for the Agency to exercise discretion in light of its limited resources[3]. However, as noted in Mylan's petition, the review of authorized generic applications would not require the Agency to expend excessive resources. Instead, the review would be limited to identifying the distributor and manufacturer of the product and withholding final approval if a generic applicant is eligible for 180-days of generic drug exclusivity.

Under any reasonable interpretation of the FDCA, the FDA's failure to prevent the marketing of this authorized generic during Mylan's 180-day exclusivity unlawfully interferes with Mylan's statutory entitlement. P&G and/or Watson did not obtain proper pre-distribution FDA authorization, under 21 C.F.R. § 314.70(b), to market this drug, as fully explained in Teva's Citizen Petition, filed with the FDA on June 9, 2004, and a copy of which was filed in support of Mylan's Petition ("Teva's Petition").

In any event, the FDA's regulations concerning changes to an approved NDA, 21 C.F.R. § 314.70, are permissive in nature, and do not *authorize* the marketing of a relabeled Macrobid, at generic prices, during Mylan's 180-day exclusivity for that drug, for the purpose of nullifying Mylan's statutory entitlement under 21 U.S.C. § 355(j)(5)(B)(iv). Stated otherwise, the FDA's regulations concerning changes to an approved NDA, 21 C.F.R. § 314.70, cannot be read in isolation, and without proper regard to the purpose of the Hatch-Waxman Amendments. In this regard, Mylan incorporates by reference the arguments in Teva's Petition.

***Authorized Generics Are Not Pro-Competitive***

Contrary to what J&J asserts, there is no evidence that authorized generics benefit consumers. No pricing data currently supports the bald assertion that authorized generics lower prices at a consumer level. In any event and most importantly, authorized generics provide a disincentive to file ANDAs with paragraph IV certifications as the exclusivity benefit will be eroded by the brand companies unlawful attempt to extent its monopoly. In the case of multiple applicants filing an ANDA on the same day and potentially being entitled to share exclusivity, the ANDA applicants entitled to exclusivity have all invested time, energy and resources in invalidating a patent or launching a non-infringing version of an approved product. The authorized generic does an end-run on the exclusivity provisions and obtains the benefit of exclusivity without any of the cost.

Moreover, the motivation of brand name companies in entering into authorized generic agreements is not to foster competition, but to deter generic competition. As explained by Chief Executive Officer of a major brand name company:

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[3] The rationale provided by the FDA for implementing section 314.101 is to prevent the FDA from having to unnecessarily expend its limited resources to conduct substantive reviews of essentially duplicative applications. *See* ANDA Regulations, 57 Fed. Reg. 17950 (Final Rule 1992) ("To permit applicants to force review of an application for a product that is already approved would result in a severe drain on FDA resources to review duplicate applications, create duplicate product and patent listings in the Orange Book, and contribute to the agency's accumulation of applications.").

> As we are looking toward the expiry of the patent on Paxil or Wellbutrin, we have picked a partner...The idea was somebody has a six month exclusivity, but we are king maker; we can make a generic company compete during the very profitable time.
>
> We are not a generic company, and do not wish to become one. If we acquired the most successful generic company in the world, it would barely move the needle on profit.[4]

If the Agency does not exercise its authority, the consumers will be the ones who are ultimately sacrificed in this game of "king maker". Under J&J's rationale, brand companies will begin entering into numerous authorized generic arrangements for the same product which will definitely lead to fewer ANDA filings and especially paragraph IV challenges.

**The FDA's Delay in Responding to the Petition Is Causing Irreparable Harm to Mylan**

As a result of P&G's and Watson's marketing of authorized "generic" Macrobid, Mylan has been deprived of its exclusivity entitlement under the FDCA, and Mylan has suffered, and continues to suffer, damages in the form of lost nitrofurantoin sales and profits at the hands of P&G and Watson. Moreover, as the first generic version of a drug usually enjoys a lasting competitive advantage by virtue of its head start, P&G's and Watson's marketing of an authorized "generic" Macrobid during Mylan's 180-day exclusivity has caused, and continues to cause, irreparable harm to Mylan.

As a result, the FDA's continued delay in answering Mylan's petition impairs the 180 days of generic exclusivity to which it is entitled under the FDCA in respect of generic nitrofurantoin. For this reason, Mylan urges the FDA to respond to its petition immediately, and in no event later than July 6, 2004.

Given the significant damages that Mylan incurs daily as a result of the marketing of P&G's and Watson's authorized "generic" nitrofurantoin, Mylan would consider the FDA's failure to respond to its petition by this date to be unreasonable and capricious, and to amount to a denial of its petition. Mylan reserves all of its rights against the FDA in connection with such a denial, including under Administrative Procedure Act, 5 U.S.C. § 706.

[4] Statement of J.P. Garnier, GlaxoSmithKline's CEO, GSK Q4 2003 Earnings Conference Call and Presentation-USA (Feb.13, 2004).

Thank you for your consideration.

Respectfully Submitted,

6/28/04
Date

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